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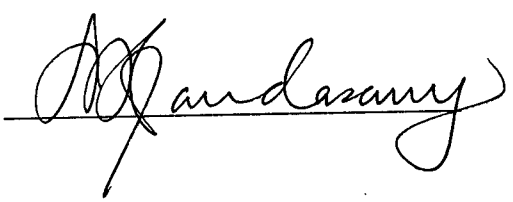

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13. ABSTRACT ***(Maximum 200 Words)***

This prospective, longitudinal study examines contraceptive outcomes among active-duty military and civilian women who receive one of three different methods of contraception (Depo-Provera, Ortho-Novum 1/35 and Ortho-Cept). Outcomes to be examined include method continuation, satisfaction, dysmenorrhea, menstrual bleeding, pregnancy rates, bone density and plasma lipids. This summary report details the specific activities that have occurred during Year 4 of funding (September 23, 1999 to September 22, 2000). According to the SOW, 3 major objectives and related tasks were to be addressed during this period. Significant progress across each major objective was achieved. A total of 386 women (183 at WHMC and 203 at UTMB) were successfully enrolled and completed their initial visit. Followup visits at 3-, 6-,. 12-, 18-, and 24-months have been conducted on 319, 262, 191, 166 and 129 subjects respectively. Preliminary analyses for data up to the 12-month visit has begun. In addition, 2 abstracts presented to major gynecologic societies have resulted from this project during year 4.

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Abby Berenson MD 10/12/00

PI – Signature Date

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Introduction

Operation Desert Shield/Storm involved the largest network of female soldiers from the United States ever deployed to a combat situation (1–3). Utilization data collected in one evacuation hospital found that 25% of all patient visits during the period of deployment were made by servicewomen, despite the fact that only 8% of the entire deployed force was female (2). Over 50% of all visits made by women were for gynecologic concerns as contraception, dysmenorrhea, and pelvic pain (3). In fact, 56% of medical evacuations by women were due to pregnancy (2). Relative to treatment, the continuation of or restarting of oral contraceptive pills and related bleeding disorders represented the largest number of gynecological complaints treated by this facility (3). These data demonstrate the critical need to determine the safest, most convenient, and most effective contraceptive method for women serving in the Armed Forces.

Two alternative forms of contraception which may be appropriate for use by servicewomen have recently been approved for use in the United States. In the past, most servicewomen requesting contraception have been prescribed a monophasic norethindrone-containing birth control pill (NOCA). In 1992, injectable depot medroxyprogesterone acetate (DMPA) received approval and more recently, birth control pills using the new progestin, desogestrel (DOCA), have been made available in the United States (12-14). As described below, these new formulations, when compared with the pill traditionally prescribed for servicewomen, may increase contraceptive efficacy and long-term continuation rates, as well as minimize dysmenorrhea and menstrual bleeding irregularities.

DMPA is an injectable progestational agent that offers a highly effective, safe, convenient, reversible and almost user-independent method of birth control (12). After a deep gluteal or deltoid injection of 150 mg, contraceptive plasma levels are reached within 24 hours, and peak plasma concentrations of 15-25 micrograms/ml are achieved within 20 days (12). Microcrystals are suspended in an aqueous solution that results in delayed absorption from the injection site and consequently prolongs the circulating concentration of the active progestin (12). Thus, effective plasma concentration for this birth control

method is sustained for at least 14 weeks, and ovulation is suppressed, on the average, for 18 weeks (12).

DOCA is a highly selective gonane progestin that has been approved for use in the United States in a monophasic formulation containing 150 micrograms of desogestrel and 30 micrograms of ethinyl estradiol (13,14). Desogestrel was one of the three new progestational agents synthesized from levonorgestrel that were developed and brought into clinical trials during the late 1970s (13). Although new to the U.S. market, DOCA has been used for almost a decade and is the most widely prescribed oral contraceptive pill in Europe. The available literature on this new formulation demonstrates that this new preparation is effective and well tolerated by most women (13,14).

Although each of these new methods of contraception may have unique contraceptive and health benefits for servicewomen, data comparing outcomes are not available. To achieve the specific aim set forth in this proposal, we will compare these contraceptives on selected outcomes (method continuation, satisfaction, dysmenorrhea, menstrual bleeding, pregnancy prevention, bone density, and plasma lipid levels) believed to be most critical for women serving in the Armed Forces.

Contraceptive Continuation. Although the continuation rate of pill use is reported in contraceptive textbooks to be 75% after 12 months of use (7,15), this figure is misleading. Most likely, this rate is inflated because it is based on the responses of married women whose contraceptive practices may be more consistent than a more diverse group of sexually active women (16,17). A more accurate estimate of pill continuation rates may be obtained by reviewing data from clinical trials that sample a more representative pool of women. Data from DOCA trials demonstrate that approximately 65% and 50% of women continued use of these pills for 12 and 24 months, respectively (18,19). Furthermore, these studies and others note that intermenstrual bleeding (breakthrough bleeding and spotting) is a common reason for pill discontinuation (13,14,18,19). Because decreased rates of intermenstrual bleeding have been reported with use of DOCA, higher rates of contraceptive continuation are believed to occur with this method as compared to more traditional birth control pills (13,14). Clinical trials conducted with DMPA suggest that continuation rates with this method are even higher (80% at 12 months and 68% at

24 months) than those observed with the traditional or newer forms of oral contraceptives, perhaps because it is easy to use or because it induces amenorrhea (12,20-26). To date, however, no study has directly compared continuation rates among these different methods of contraception. The present proposal will help fill this void by systematically examining rates of continuation among three different methods of hormonal contraception after 6-, 12-, and 24-months of use.

Method Satisfaction. Factors which may influence user satisfaction and lead to contraceptive discontinuation include menstrual irregularities, weight gain, nausea, headaches, mood changes, dizziness, acne, fatigue, and breast swelling or tenderness (7,27,28). Generally, discontinuation rates due to side-effects other than menstrual irregularities are less than 4%, but can vary according to method (27,29,30). One medical side effect of particular concern to many women is weight gain. Continuous weight gain has been associated with the progestin component of hormonal contraceptives (31). Double-blinded studies among different pill formulations suggest there is little evidence that oral contraceptive use leads to increased weight (29,30). In contrast, DMPA use results in an average gain of 2-3 lb. per year (31). This side effect may be of particular concern to women serving in or planning to serve in the military, as those who gain weight secondary to contraceptive use may not meet the required weight/height physical standards unique to their branch of the armed forces after long term use. Although consistent exercise may help control this weight gain, a willingness to exercise may be impeded by DMPA use as preliminary studies suggest that this method results in increased fatigue (32).

Other issues that affect satisfaction relate to symptom improvement as a result of a particular hormonal method. For example, DOCA usually improves acne skin conditions among users. In one study of DOCA users, a significant proportion of women with acne reported complete resolution of this problem (13,14,19). Another benefit of oral contraceptives, especially DOCA, is the effect on hirsutism (13,14,19). Several studies employing this newly available oral contraceptive have reported significant improvement of this condition after 6 months of continued use. Unfortunately it is difficult to interpret data on method satisfaction from prior contraceptive studies because increased satisfaction with a method is usually inferred from a lack of reported medical side-effects by subjects, rather than by use of

specific questions to inquire about satisfaction. For example, most women who participated in the multicenter clinical trials on DOCA reported excellent cycle control, reduced intermenstrual bleeding and spotting, and among women with dysmenorrhea, reduced symptomatology (13,19) Moreover, at 6-, 12-, and 24-months of use, about 88%, 92%, and 94%, respectively, of the sample did not report any medical side-effects (19). Thus, researchers concluded that a high degree of method satisfaction, and therefore continuation, existed for those women taking this newly formulated pill (13,14,19). Investigators of DMPA found that about 64% of women did not report any medical side-effects (and thus were satisfied) in any one year during a five-year follow-up evaluation (23). Unfortunately, variations in study methodology have made it difficult to compare user satisfaction across studies and no single study has compared method satisfaction across different methods of contraception. This study will help fill this void by systematically evaluating method satisfaction including medical side-effects after 6-, 12-, and 24-months of use.

Dysmenorrhea. One of the single, largest causes of periodic absenteeism and decreased work productivity among young civilian women is dysmenorrhea (5-10). Pain with menstruation, or dysmenorrhea, represents a common gynecological complaint affecting approximately 70% of young women (5-10). Fifteen percent of young adult women who report pain with menstruation state that it is severe enough to limit usual activity even when analgesics are used (6). This disorder is commonly treated with combined oral contraceptive pills. However, 30% of women given traditionally formulated pills continued to experience moderate to severe dysmenorrhea (9). Studies of DOCA suggest that this new formulation may be more beneficial than traditional pills in ameliorating dysmenorrhea, perhaps due to a decrease in breakthrough bleeding episodes (19). For example, an open cross-over study on women with primary dysmenorrhea which did not respond to traditional pills noted that a significant number who used DOCA for 3 months reported reduced pain and 80% of the sample wished to remain on this pill formulation (10). Another study found that 50% of women taking DOCA reported significant improvements in their dysmenorrhea after using this formulation of one month (19).

Traditionally, the therapy for dysmenorrhea has been the oral contraceptive pill because it reduces the prostaglandin content of menstrual fluid and therefore decreases uterine motility (5-10). However, specific comparative studies examining treatment efficacy of various contraceptive regimens have not been conducted. Although the etiology of dysmenorrhea has yet to be clearly elucidated, it is suspected that the amelioration of dysmenorrheic symptoms is due to the suppression of ovulation (9). Data collected from clinical DMPA trials has found that up to 70% of users are amenorrheic after 4 or more injections. Thus, if cessation of ovulation results in decreased symptoms, long-term use of DMPA may provide greater benefit than any pill formulation.

Menstrual Bleeding. All hormonal contraceptive methods affect the menstrual cycle and may influence the pattern and amount of bleeding (33). Contraceptives generally affect the menstrual cycle in one of 2 ways: (1) cyclic bleeding continues, as with oral contraceptive pills, where the hormonal formulation substitutes an artificial cycle for the woman's own cycle, but withdrawal bleeding occurs during the last 5-7 days; or (2) the normal cycle is partially or completely suppressed and the method does not induce cyclic bleeding, as with DMPA (33).

Irregular bleeding may also occur with use of hormonal contraception. However, the frequency of intermenstrual bleeding tends to decrease with continued use. Unfortunately, many clinical trials, especially those conducted 5 or more years ago, do not report their bleeding rates in a standard fashion, i.e., across 90-day reference periods (number of bleeding, spotting, and nonbleeding episodes that are summed across a 90-day period). Thus, data cannot be directly compared between formulations. Nonetheless, data collected on clinical trials of DOCA suggest a marked reduction in breakthrough bleeding (BTB) and spotting (14). Although BTB is more prevalent in the first few cycles of use (1.2-10%), by the sixth cycle, reported rates have decreased to 0.4-9.2% among users (14). With regard to spotting, rates are reported to decrease from 18.2% at cycle 1 to 5.8% by cycle 6 (14). In contrast, DMPA users commonly report episodes of unpredictable spotting and bleeding lasting seven or more days during the first few months of use. Data collected from an efficacy study found that the average number of bleeding or spotting days per 90-day reference period was 24.2 at 3 months, 18.5 at 6 months,

10.7 at 12 months, 7.6 at 18 months, and only 6.8 days at 24 months (26). However, as women continue with this hormonal method, amenorrhea becomes common. More than 70% of women develop this condition after 4 or more injections (12). This may be of particular benefit during periods of deployment. This study will directly compare the number of bleeding days associated with use of three different hormonal methods.

Pregnancy Prevention. Unplanned pregnancy among military servicewomen accounts for a significant number of hospital visits and loss of work productivity. As previously stated, pregnancy was the single largest cause of medical evacuation out of the theater during Operation Desert Shield/Storm (3). A longitudinal investigation of Navy women who enlisted between 1973 and 1987 found that for the first year of active-duty, the highest rates of hospitalization for the 1973-77 cohort was for induced abortion, while complications of pregnancy represented the highest hospitalization rate for the 1983-87 cohort (34). Moreover, pregnancy-related conditions continued to contribute to high levels of hospitalization for the remainder of this five-year active-duty interval. With the increase of female soldiers in combat areas, it will also be critical to protect personnel who are taken prisoner from becoming pregnant as a result of rape as recent conflicts demonstrate that this act is increasing as a crime of war (35).

Used consistently and correctly, the monophasic norethindrone oral contraceptive has a theoretical efficacy rate of 99% (27). However, the actual occurrence of pregnancy is as high as 8% due to poor daily compliance (36). Contraceptive management to ensure daily adherence is challenging because noncompliance may not be a willful, conscious act. More frequently, it is due to forgetfulness or misunderstanding of when to initiate pill use or what to do when a pill is missed (27,28). In contrast, DMPA is almost user-independent. A recent cost-benefit analysis conducted for pregnancy prevention compared DMPA with two different birth control pills and Norplant® (37). These researchers reported that among pill users, the actual contraceptive efficacy was 95% versus 99.7% among DMPA users and concluded that DMPA delivered the highest net benefit for pregnancy prevention.

Bone Density The evaluation of hormonal effects on bone density are critical to the military, because a high incidence of musculoskeletal injuries, including stress fractures, have been reported among females in the eight weeks of basic training (38), and similar problems are likely to occur in combat situations. One particular concern with the use of DMPA by military women, therefore, is the suggestion that it may adversely affect bone density. A recent study examining bone density changes in women who had used DMPA for 5 or more years found reduced lumbar spine and femoral neck densities, compared to findings in premenopausal controls (39). However, these data are somewhat difficult to interpret because the study sample was considerably older (most in their mid-40s), and over half were smokers, factors that have been shown to contribute to loss in bone density.

In contrast, three cross-sectional studies and one longitudinal study have shown that NOCA favorably affects bone mass (40-42). For example, Lindsay et al (40) examined two groups of women aged 25 to 33 years who had variable health histories and found a 1% gain in bone density occurred for each year of pill use. DOCA has been associated with maintenance of bone mass in two separate studies (14,43). Ricci, Mango, Manna, et al. (43), examined the effects on bone mass density among 17 nulliparous women who had never taken oral contraceptives. These researchers found that bone density after one year of use was comparable to pretreatment levels. Another study employing a slightly different formulation (20 micrograms of ethinyl estradiol) conducted in Italy examined premenopausal women and reported a preservation of bone mass after two years of use (44). These authors conclude that DOCA does not appear to have any deleterious effects on bone density, but does not offer any protective effects for fracture rates either. Thus, it appears that no harmful effects on bone density result from oral contraceptive use and in some premenopausal women using pills, positive effects may result.

Plasma Lipid Levels. A "perfect" hormonal method of birth control would neither increase plasma levels of total cholesterol and low density lipoprotein (LDL) nor reduce high-density lipoprotein cholesterol (HDL) (45). However, the estrogen component of traditionally formulated oral contraceptives usually raises HDL-cholesterol and triglycerides levels (18) while the progestin component has the opposite effect and tends to lower HDL-cholesterol (18). The importance of such

changes in the genesis of arterial vascular disease in users of oral contraceptives is not clear, but presents some cause for concern (45). Although a definitive study examining these concerns has not been conducted, it is generally believed that plasma lipid level changes are likely related to the specific type and dose of progestin employed (7). For example, one study comparing two groups of women taking triphasic formulations (Ortho-Novum® 7/7/7 and Triphasil®) with non-contracepting controls found significant increases in total plasma cholesterol, LDL-cholesterol, and triglycerides levels after 6-months of use (45). Triglyceride levels declined by 12-months, but total- and LDL-cholesterol levels maintained these elevations at one year. HDL-cholesterol was not significantly different after 6- or 12-months of use. Although these researchers found statistically significant differences between women on pills compared to nonusers, all values were within acceptable clinical or normal ranges (45). Thus, the authors conclude that any contribution to increased atherogenesis by either formulation is highly unlikely.

A recent review of more than 50 clinical studies employing DOCA report that this new formulation did not interfere with estrogen's effects on lipoprotein metabolism (13). Although data suggest that statistically significant increases in HDL-cholesterol were found, LDL-cholesterol remained unchanged or demonstrated a slight reduction (13). Another study examining nine groups of women using different oral contraceptives with non-contracepting controls found that levels of LDL-cholesterol were reduced by 14% in those taking pills containing desogestrel and by 12% in those taking low-dose norethindrone (44). Furthermore, these researchers found that the pills traditionally prescribed by the military (NOCA), which contain high-dose norethindrone, did not affect HDL-cholesterol levels, whereas those taking DOCA had increased their HDL by 12% (46). However, duration of oral contraceptive use in this study varied from 3-months to 4-years rendering specific conclusions difficult to interpret.

Conflicting findings on plasma lipid levels among DMPA users have been reported (12). In one study examining the long-term use (5-12 years) of several different contraceptive methods, DMPA caused a moderate decrease in triglycerides, HDL-cholesterol, and apoproteins, whereas estrogen-dominant pills (2 mg norethisterone, 0.1 mg mestranol) increased these same parameters (47). Some

investigators have concluded that long-term use of this agent includes some change in lipid metabolism that would be considered a risk factor for atherosclerosis (48).

Technical Objectives

The broad aim of this proposal is to provide critical data on contraceptive outcomes that may be used to generate reproductive healthcare guidelines for servicewomen who have varying needs depending on their military assignment. To accomplish this goal, we are using a prospective, longitudinal design, to compare outcomes among three different methods of contraception (NOCA, DOCA, and DMPA) and are recruiting participants from both military and civilian sites. Use of a nonmilitary site allows us to collect data from women whose health status and reproductive needs are likely to mirror those of reservists and new recruits. Each contraceptive condition will be comprised of approximately 150 women aged 18 to 33 years: one half are being recruited from active-duty servicewomen from one of five military bases in San Antonio and receive their care at Wilford Hall Medical Center, San Antonio, Texas and the remaining half are solicited from women in the greater Galveston-Houston area and receive their at either UTMB's Maternal and Child Health clinic in Galveston, Texas, or a satellite clinic in Webster, Texas. All potential civilian women must meet entry standards for the Armed Forces. All study participants are being assessed after 3-, 6-, 12-, 18-, and 24 months of contraceptive use.

At follow-up visits, subjects complete standardized measures of dysmenorrhea, menstrual pain, medical side-effects and method satisfaction, and submit completed monthly menstrual calendars. Physical examinations are performed by a nurse practitioner or physician at entrance into the study and after 12- and 24-months of continuous contraceptive use. In addition, bone density measurements (lumbar spine and femoral neck) using dual x-ray absorptiometry (DEXA) are obtained at baseline and the 24-month assessment, while lipid levels are being assessed at baseline and after 12- and 24-months of contraceptive use. DMPA participants return to the clinic at 9, 15, and 21 months to receive an injection only. The specific technical objectives of this study are to determine, at the conclusion of 2 years, which of these three methods:

1. has the highest rate of continuation;
2. has the highest level of user satisfaction;

3. most effectively reduces the occurrence and severity of dysmenorrhea;
4. most effectively decreases the number of bleeding days per 90-day reference period;
5. has the lowest user failure rate resulting in pregnancy;
6. minimizes bone density loss;
7. minimizes changes in lipoprotein levels; and
8. minimizes the occurrence medical side-effects.

Data will be analyzed employing repeated measures multivariate statistical tests so that (1) trends in outcomes over 24 months of contraceptive use can be examined; (2) comparisons of outcomes at specific points in time (6, 12, and 24 months) may be performed; and (3) main effects for method, time, recruitment site, and their interactions can be evaluated. The results of these analyses will help determine the safest, most convenient, and most effective contraception for servicewomen in various phases of duty, i.e., deployed and nondeployed. For example, women who are deployed for two years may experience more contraceptive and noncontraceptive benefits (few bleeding days) as well as greater long-term satisfaction with an injectable contraceptive as compared to an oral contraceptive. In contrast, non-deployed servicewomen with severe dysmenorrhea may experience the greatest relief from DOCA, and hence have reduced absenteeism.

Body

This fourth summary report details the specific activities that have occurred during Year 4 of funding (September 23, 1999 through September 22, 2000). According to our Statement of Work, there are a total of 5 major objectives. All tasks in Objectives 1 and 2 were initiated and completed during the first 36 months of the granting period and are not reported in this summary. Thus, three major objectives and related tasks were to be completed during the fourth 12 months of funding. Objectives three through five consist of completing required medical assessments, laboratory tests, and self-report and satisfaction measures at each visit; analyze preliminary study data and complete the yearly annual report. The progress on each objective is addressed in this report.

Objective 1: Implement the study protocol.

This objective and tasks 1 – 6 were completed in year 1 of funding and reported in the first summary report.

Objective 2: Establish the three contraceptive cohorts: users of norethindrone-containing pills (NOCA), desogestrel –containing pills (DOCA), and DMPA.

This objective and tasks 1 through 7 were completed in year 3 of funding and reported in the third summary report.

Objective 3: Complete required follow-up medical assessments, laboratory tests, and self-report and satisfaction measures at each visit.

Activities associated with this objective are designed to maintain the research cohort. Ten tasks are associated with achieving this objective and include: 1) order, prepare, and xerox required study forms as well as appointment reminder post cards; 2) prepare and mail appointment reminder postcards to each participant; 3) perform tracking procedures on participants whose appointment reminder cards were returned undelivered; 4) compensate UTMB subjects for their participation in the study at each follow-up visit and contact via phone all discontinuers; 5) dispense oral contraceptives or administer Depo-Provera and count unused or missed birth control pills; 6) complete brief medical visit and satisfaction/side-effect measures at the 3-month follow-up visit; 7) complete brief medical visit and satisfaction/side-effect measures at the 6-month follow-up visit; 8) complete yearly medical visit including satisfaction/side-effect measures, and blood tests; 9) complete brief medical visit and satisfaction/side-effect measures at the 18-month follow-up visit; and 10) complete final visit which includes satisfaction and side-effect measures, well-women examination, laboratory tests, and bone density scan. Each of these tasks has been accomplished. Data reported in this summary includes visits completed by September 1, 2000.

Task 1. ***Order, prepare, and xerox required study forms as well as appointment reminder post cards.*** This task was completed in year 1 of funding and was reported in the first summary report.

Task 2. ***Prepare and mail appointment reminder cards to each participant.*** At the conclusion of each subject's visit, she is provided with an appointment for her next follow-up visit. A reminder letter is generated from our electronic database 14 days prior to her appointment. Each subject in

addition is called one day before her scheduled appointment to be sure the patient is able to complete the appointment.

Task 3. ***Perform tracking procedures on participants whose appointment reminder cards were returned undeliverable.*** During the fourth year of funding, 6 reminder letters were returned as undeliverable. In these cases, tracking procedures by phone were implemented. Multiple attempts to reach the 6 subjects by phone, mail, or through family or friends have been unsuccessful to date. Thus, a total of 12 subjects (2 in Year 2, 4 in Year 3, and 6 in Year 4) did not complete their scheduled visit as we were unable to locate them. This represent a lost-to follow-up rate of 3.2% (12/386).

Task 4. ***Compensate UTMB subjects for their participation in the study at each follow-up visit and contact via phone all discontinuers.*** All subjects at UTMB who have returned for follow-up visits have received compensation each visit. Subjects recruited at WHMC cannot receive compensation per installation policy. At this time, 115 subjects at UTMB and 107 subjects at WHMC elected to discontinue their chosen contraceptive method. Of the 107 subjects at WHMC, 89 have completed the discontinuation survey. The remaining 18 subjects will complete the questionnaire by phone in the next 5 months. A total of 58 subjects at UTMB have either completed the survey or will complete it in the next 4 months. Data on 57 subjects who discontinued at UTMB is unavailable as the subject either refused to complete the survey (N= 40) or moved away after discontinuing the study (N=17).

Task 5. ***Dispense oral contraceptives or administer Depo-Provera (DMPA) and count unused or missed birth control pills.*** At 12, 18 and 24 month visits, all women assigned to either pill condition received a supply of pills and were instructed to continue their use. During the reminder phone call about the scheduled appointment, pill users are also asked to bring in their pill packs. Each pill package was numbered according to the month it is to be used, and counts of all missed pills are recorded on the Nursing Assessment scannable form. With regard to DMPA users, subjects have continued to return to the clinic to receive their injection every 90 days after their initial injection. To date, all subjects using this birth control method have received their follow-up injection within 2 weeks of their scheduled appointment.

Task 6. ***Complete brief medical visit and satisfaction/side effect measures at the 3-month follow-up visit.*** This task was completed during Year 3 of funding and reported in the third summary report.

Task 7. ***Complete brief medical visit and satisfaction/side effect measures at the 6-month follow-up visit.*** This task was completed during Year 3 of funding and reported in the third summary report.

Task 8. ***Complete yearly medical visit including satisfaction, side effects measures, and blood tests at the 12-month follow-up visit.*** One hundred ninety-one (191) subjects completed the 12 month follow up visit. This visit included a well-women exam consisting of a general physical examination with pap smear and blood work for Cardiac Risk Panel and Coulter Profile. Cultures for sexually transmitted disease were taken routinely at UTMB as standard of care. WHMC performs STD cultures only if indicated. Subjects also completed the self-report measures of satisfaction, dysmenorrhea, and medical side-effects. In addition, menstrual calendars were reviewed and the number of missed pills counted by the medical provider. All 12 month follow-up visits at both sites are now completed.

Task 9. ***Complete brief medical visit and satisfaction/side effect measures at the 18-month follow-up visit.*** One hundred sixty-six (166) subjects have completed the 18-month visit. At this visit, the self-report measures of satisfaction, dsymenorrhea, and medical side effects were completed. In addition, menstrual calendars were reviewed and the number of missed pills counted by the medical provider. All 18 month follow-up visits at both sites are now completed.

Task 10. ***Complete final visit which includes satisfaction and side-effect measures, well-woman examination, laboratory tests, and bone density scan.*** One hundred twenty-nine (129) subjects have completed the final visit. Some subjects at UTMB who completed this visit did not receive a well-woman examination (N=13), as they elected to receive this service from their private physician. All remaining subjects underwent a well woman examination which includes a general physical exam with Pap smear. In addition, blood was obtained for a Cardiac Risk Panel and Coulter Profile from all subjects regardless of whether or not the pelvic examination was done. Cultures for sexually transmitted

disease were taken routinely at UTMB as standard of care. WHMC performs STD cultures only if indicated. Subjects also completed self-report measures of satisfaction, dysmenorrhea, and medical side effects. In addition, menstrual calendars were reviewed and the number of missed pills counted by the medical provider. Table 1 below outlines the number of medical visits by follow-up date for both UTMB and WHMC as of September 01, 2000.

Table 1. Follow-up medical visits completed by site.

Visit Type	UTMB	WHMC
3-Month	171	148
6-Month	144	118
12-Month	107	84
18-Month	88	78
24-Month	76	53

Objective 4: Analyze study data

This objective involves quantifying study results. There were 9 tasks identified for this objective relevant to year 4: 1) develop and pilot the database for collected data; 2) develop and finalize the accuracy of importing menstrual calendars and related self-report questionnaires for the database; 3) conduct reliability analysis on 10% of medical visits; 4) perform all data entry and verification of study data; 5) reconcile out-of range and inconsistent data elements to insure accuracy of the study data; 6) perform preliminary analyses; 7) present preliminary findings; 8) complete all data entry, range checks, and perform final analyses; and 9) prepare and present reports.

Task 1. ***Develop and pilot database for collected data.*** Separate databases for each of the 6 time points (baseline, 3,6,12,18, and 24 months) have been developed.

Task 2. ***Develop and finalize accuracy of importing menstrual calendars and related self-report questionnaires for database.*** Definitions and rules were developed for the recording of the menstrual calendar data. A data collection instrument was designed and is currently in use (Appendix A). Data resulting from the menstrual calendars includes the following for each 90-day reference period; (1) range of bleeding/spotting episodes; (2) range of spotting only episodes; (3) range of nonbleeding episodes; (4) the longest bleeding episode; (5) the longest spotting episode; (6) the longest

nonbleeding interval; (7) the total number of bleeding/spotting days; (8) the total number of spotting only days; and (9) the total number of nonbleeding days. To date 148 menstrual calendars have been coded and entered into an electronic database. Two hundred and thirty-eight menstrual calendars will be coded and entered in the coming months.

Task 3. ***Conduct reliability analysis on 10% of medical visits.*** We exceeded our goal of conducting a reliability analysis of 10% of visits. An analysis of 298 of 1,417 visits is completed. This represents 21% of the total visits. Reliability across these visits is excellent at 93%.

Task 4. ***Perform all data entry and verification of study data.*** Software programs to electronically scan computer-ready questionnaires of the four self-report measures were completed in year 3. Data entry and verification for all data up to 12 months has been completed (See Table 2).

Table 2. Data entry, verification, and cleaning of data.

Tasks	3 mo. data	6 mo. data	12 mo. data	18 mo. data	24 mo. data
Scan forms	X	X	X	X	IP
Upload to SPSS	X	X	X	X	
Reconcile missing data	X	X	X	IP	
Ready for analysis	X	X	X		

KEY: X = Completed; IP = In progress

Task 5. ***Reconcile out-of-range and inconsistent data elements to insure accuracy of study data.*** All forms are visually inspected as the subject completes the form to insure the accuracy of collected data. Out of-range evaluation is conducted at the time the visit-specific databases (baseline, 3-, 6-, 12-, 18-, and 24-month) are assembled. Out of range evaluation has been completed on all data up to the 18-month visit. Scanning for the 18-month data is completed and reconciliation of the missing data is currently in progress. The scanning of the 24-month data has started. Twenty-nine final visits are outstanding and will be completed in the next three months.

Task 6. ***Complete all data entry, range checks, and perform final analyses.*** Data entry and verification for all data up to 18 months has been completed. Final analyses will begin at the end of the first quarter of 2001 when all the study visits have been completed.

Task 7. ***Perform preliminary analyses.*** Preliminary univariate analyses of the data through the 12 month visit is currently in progress. See section Reportable Outcomes on page 23.

Task 8. ***Presentation of preliminary findings.*** To date two abstracts from these data have been accepted for presentation at national meetings.

1. **A prospective study of the effects of oral and injectable contraception on bone mineral density.** This abstract was presented orally at the American College of Obstetricians and Gynecologists on May 22, 2000 (Obstet Gynecol 2000; 95: S6).

In this abstract, data on 100 women who participated in this study was evaluated to compare the effects of the three different hormonal contraceptives (injectable depot medroxyprogesterone acetate (DMPA), norethindrone-containing oral contraceptives, or desogestrel-containing oral contraceptives) on bone mineral density (BMD) in reproductive age women.

BMD was measured by dual energy x-ray absorptiometry at baseline and after one year of contraceptive use. Data on other factors that could affect BMD (smoking status, alcohol use, body mass index, exercise habits, and race) were obtained by interview or examination. An analysis of covariance was performed to test for differences in BMD among the three groups after one year of contraceptive use, controlling for potential confounding variables.

No significant differences were noted in age, race, body mass index, smoking status, alcohol use, exercise habits or BMD between the three groups at baseline. After one year of contraceptive use, DMPA users experienced a 2.5% decrease in BMD as compared to a 2.8% increase among users of norethindrone-containing pills and a 0.9% increase among users of desogestrel-containing pills ($p<.001$). Pairwise comparisons demonstrated that these changes in BMD significantly differed between users of DMPA and norethindrone-containing pills ($p<.001$), between users of DMPA and desogestrel-containing pills ($p=.001$) and between users of norethindrone- and desogestrel-containing pills ($p=.04$).

These data demonstrate that different methods of hormonal contraception have significantly different effects, at least temporarily, on BMD after only one year of use.

2. **Condom practices prior to and after initiation of hormonal contraception**. This abstract will be presented as a poster at the Central Association of Obstetricians and Gynecologists October 21, 2000.

In this abstract, data on 310 women who participated in this study was evaluated to examine condom practices among women of reproductive age not using hormonal contraception and identify factors associated with condom use 3 months after initiation of hormonal contraception.

At recruitment, all women completed a detailed questionnaire eliciting information on demographic and reproductive characteristics, condom use during the past 3 months, and attitudes toward condom use. Demographic information obtained included age, race/ethnicity, marital status, employment status, and family income, while reproductive information included gravidity, parity, number of sexual partners during the past 3 months, number of sexually transmitted diseases (STD) in their lifetime, and age at initiation of sexual intercourse. Questions about condom practices in the last 3 months included how frequently they had used a condom (every time, most of the time, often, sometimes, or never) and number of times they refused to have sex if a condom was not available (never, ≥1 time). Attitudes toward condom use were measured using the Multidimensional Condom Attitudes Scale. Logistic regression analyses were conducted on baseline data to identify demographic and attitudinal predictors of condom use and refusal of sex due to lack of a condom. Additional analyses were undertaken to examine changes in condom practices subsequent to initiation of hormonal contraception and to identify predictors of discontinued use.

Data were available on 310 women at baseline. The mean age of participants was 24.3 ± 4.0 years. Two-thirds of the sample was unmarried. Twenty-three percent reported that they had a STD in the past.

At baseline, only 23% (72/310) of women reported that they used a condom every time they had sexual intercourse during the past 3 months. Twenty-nine percent (89/310) of women stated that they had refused to have sexual intercourse at least once in the past 3 months because a condom was not available. Women who used condoms every time they had sex were more likely to be unmarried (OR = 2.4, 95% CI = 1.2 to 5.1), to have a family income <$30,000/ year (OR = 2.6, 95% CI = 1.3 to 5.3), and express beliefs that condoms did not interfere with sexual pleasure (OR = 2.2, 95% CI = 1.3 to 3.5). Women who refused to have sex because a condom was not available were more likely to be Hispanic

than White (OR = 3.3, CI = 1.3 to 7.5), to be unmarried (OR = 2.3, 95% CI = 1.1 to 4.5), to have >1 sexual partner (OR = 2.6, 95% CI = 1.3 to 5.1), and to believe that condoms do not interfere with sexual pleasure (OR = 1.5, 95% CI = 1.0 to 2.3). In addition, women who refused to have sex were less likely than those who did not refuse to believe that condoms are reliable and effective (OR = 0.65, 95% CI = 0.43 to 0.97). No relationship was observed between condom practices and history of a STD, age, gravidity, parity, employment status, or age at initiation of sexual intercourse. Furthermore, no relationship was observed between condom practices and attitudes surrounding the purchase, negotiation and use, or stigma associated with condoms.

A total of 299 women completed a follow-up survey 3 months after initiating hormonal contraception. Overall condom use declined after initiation of hormonal contraception: only 14% (41/299) of women reported using them at every sexual encounter at 3 months. Similarly, the overall percentage of women who refused to have sexual intercourse because a condom was not available declined from 29% at baseline to 15% (45/308) at 3 months. Unmarried women who changed their condom use after initiating hormonal contraception (N = 44) were significantly more likely to discontinue using condoms after initiating hormonal contraception than to begin using condoms (33/44 vs. 11/44; P < .001). Logistic regression analyses identified only one factor as a significant predictor of condom discontinuation: women with a family income <$30,000/year were nearly three times more likely than those earning ≥$30,000/year or more to discontinue using condoms after initiating hormonal contraception (OR = 2.7, 95% CI = 1.1 to 6.8). Age, gravidity, race/ethnicity, marital status, employment status, number of partners, prior history of a STD, and age at initiation of sexual intercourse did not predict who discontinued using condoms in the multivariate analyses. Furthermore, none of the condom attitudes were associated with discontinued use.

These data demonstrate that most women do not use condoms before or after initiation of hormonal contraception. Multivariate analysis revealed that it is extremely difficult to predict who will stop using condoms, even when demographic, attitudinal and behavioral information are available. In the absence of identifiable factors which predict who will discontinue using condoms, it is critical that

clinicians assess each woman's risk of contracting a STD when hormonal contraception is prescribed and counsel women at risk of the need for concurrent condom use.

Task 9. ***Preparation and presentation of reports.*** The preliminary analysis of data up to 12 months has begun. The preparation and presentation of reports will be completed during the year of 2001.

Reportable Outcomes

As noted in the original application, the specific technical objectives of this study are to determine which of these contraceptive methods:

1) has the highest rate of continuation;
2) has the highest level of user satisfaction;
3) most effectively reduces the occurrence and severity of dysmenorrhea;
4) most effectively decreased the number of bleeding days per 90-day reference period;
5) has the lowest user failure rate resulting in pregnancy;
6) minimizes bone density loss;
7) minimizes changes in lipoprotein levels; and
8) minimize the occurrence of medical side effects.

Technical objectives 1, 2, 5, 6, and 8 are reported in this summary. Objectives 3, 4, and 7 will be completed in the coming months. The following preliminary, univariate analyses were conducted on data obtained at 6, and 12 months. Univariate analyses of baseline data was reported in the third summary report. Multivariate analyses will begin when data collection at 24 months is completed. The results of these analyses by objective are reported below.

OBJECTIVE 1) To determine which method has the highest rate of continuation (includes data up to 12 months only).

At six and twelve months of participation, the percentage of women who were still using their contraceptive method did not differ between Depo-Provera users and oral contraceptive pill users (Table 3).

Table 3. Highest rate of continuation at 6 and 12 months for each contraceptive method

	DMPA	NOCA	DOCA	p
6 months	90/138 (65%)	82/119 (69%)	90/129 (70%)	.70
12 months	68/138 (49%)	67/119 (56%)	73/129 (57%)	.40

OBJECTIVE 2) To determine which method has the highest level of user satisfaction (includes data up to 12 months only).

At six months of contraceptive use, DMPA users were significantly less likely than pill users to report that they were satisfied with their current method and significantly more likely to report experiencing negative feelings about their contraceptive method (Table 4). However, by twelve months of contraceptive use no significant differences between those who were satisfied with their method and those who experienced negative feelings about their contraceptive choice were observed between contraceptive groups (Table 5). After 6 months of contraceptive use there was no significant difference between those who would or would not recommend use of their contraceptive to friends (Table 4). After 12 months of use, however, DMPA users were significantly less likely than either pill group to recommend using their method to friends (Table 5). Additionally, DMPA users as compared to pill users were significantly more likely at both time points to state that the occurrence of side effects was more than expected (Tables 4 and 5). Both DMPA users and pill users at both time points felt that their method was easy to use and effective in preventing pregnancy (Tables 4 and 5).

Table 4. User satisfaction at 6 months.

	DMPA	NOCA	DOCA	p
Satisfied with method	72/99 (73%)	73/84 (87%)	77/92 (84%)	.04
Experienced negative feelings	37/99 (34%)	13/84 (16%)	16/93 (17%)	< .01
Would recommend method to friends	95/98 (97%)	82/83 (99%)	91/91 (100%)	.21
Occurrence of side effects more than expected	59/98 (60%)	37/84 (44%)	31/92 (34%)	< .01
Method is easy to use	98/99 (99%)	82/84 (98%)	88/92 (96%)	.34
Method is effective in preventing pregnancy	99/99 (100%)	82/84 (99%)	92/93 (99%)	.30

Table 5. User satisfaction at 12 months.

	DMPA	NOCA	DOCA	p
Satisfied with method	59/69 (86%)	58/69 (84%)	65/73 (89%)	.67
Experienced negative feelings	17/70 (24%)	8/63 (12%)	11/73 (15%)	.12
Would recommend method to friends	67/70 (96%)	69/69 (100%)	72/72 (100%)	.05
Occurrence of side effects more than expected	45/70 (64%)	31/68 (46%)	29/72 (40%)	.01
Method is easy to use	69/70 (99%)	68/68 (100%)	70/73 (96%)	.20
Method is effective in preventing pregnancy	70/70 (100%)	69/69 (100%)	73/73 (100%)	

OJBECTIVE 5) To determine which method has the lowest user failure rate resulting in pregnancy (includes data up to 12 months only).

As expected the failure rate due to imperfect use was low in all three contraceptive groups (0.1%). However, pill users were significantly more likely than DMPA users to become pregnant due to imperfect use (Table 6).

Table 6. Failure rate resulting in pregnancy

	DMPA	NOCA	DOCA	p
Experienced pregnancy due to imperfect use	0/68 (0%)	6/70 (0.1%)	4/75 (0.1%)	.05

OJBECTIVE 6) To determine which method minimizes bone density loss (includes data up to 12 months only).

No significant differences were noted in age, race, body mass index, smoking status, alcohol use, exercise habits or BMD between the three contraceptive groups at baseline. After one year of contraceptive use, DMPA users experienced a 2.5% decrease in BMD as compared to a 2.8% increase among users of norethindrone-containing pills and a 0.9% increase among users of desogestrel-containing pills ($p<.001$). Pairwise comparisons demonstrated that these changes in BMD significantly differed between users of DMPA and norethindrone-containing pills ($p<.001$), between users of DMPA and desogestrel-containing pills ($p=.001$) and between users of norethindrone- and desogestrel-containing pills ($p=.04$). These data demonstrate that different methods of hormonal contraception have significantly different effects, at least temporarily, on BMD after only one year of use. These data were presented orally at the American College of Obstetricians and Gynecologists on May 22, 2000 (Obstet Gynecol 2000; 95: S6).

Table 7. Mean change in lumbar bone mineral density after 12 months of contraceptive use.

DMPA	-2.5%
Norethindrone-containing pills (NOCA)	+2.8%
Desogestrel-containing pills (DOCA)	+0.9%

OBJECTIVE 8) To determine which method minimizes the occurrence of medical side effects (includes data up to 12 months).

Eleven side effects associated with the use of hormonal contraception were assessed at 6 and 12 months (Tables 10 and 11). DMPA users were significantly more likely at both 6 and 12 months than either NOCA or DOCA users to report > 20 days of bleeding, amenorrhea, increased appetite, and weight gain. At 6 months DMPA users were also more likely than either pill group to report intermenstrual bleeding, but by 12 months no difference in intermenstrual bleeding was observed between the groups. Additionally at 12 months of contraceptive use, DMPA users were almost 4 times more likely to report hair loss and the growth of hair on the upper lip as were either group of pill users.

Table 10. Side effects reported by DMPA users as compare to pill users at 6 months.

	OR	**CL**	**p**
>20 d of bleeding	34.0	(4.4, 261.0)	<.01
Bleeding between periods	2.0	(1.0, 3.9)	<.01
No bleeding between periods	9.0	(4.0, 18.7)	<.01
Nervousness	1.1	(0.4., 2.8)	.90
Nausea	0.6	(0.3, 1.4)	.20
Breast tenderness	0.3	(0.1, 0.5)	<.01
Decrease in appetite	1.3	(.54, 3.0)	.60
Increase in appetite	1.9	(1.0, 4.0)	.05
Weight gain	3.0	(1.4, 4.7)	.03
Diminished sex drive	2.4	(1.2, 4.8)	.01
Hair loss	1.4	(1.0, 3.5)	.50
Hair growth on upper lip	1.2	(0.5, 3.4)	.70

Table 11. Side effects reported by DMPA users as compare to pill users at 12 months.

	OR	CL	p
>20 d of bleeding	1.9	(0.8, 4.3)	.01
Bleeding between periods	1.9	(0.8, 4.3)	.14
No bleeding between periods	16.8	(5.9, 48)	<.01
Nervousness	0.7	(0.2. 2.1)	.47
Nausea	0.5	(0.2, 1.3)	.13
Breast tenderness	0.7	(0.3, 1.5)	.36
Decrease in appetite	2.6	(2.1, 3.3)	.01
Increase in appetite	2.5	(1.1, 5.5)	.03
Weight gain	2.1	(1.1, 4.2)	.03
Diminished sex drive	1.3	(0.6, 3.0)	.52
Hair loss	3.7	(1.1, 13.1)	.03
Hair growth on upper lip	3.7	(1.1, 13.1)	.03

Key Research Accomplishments

During this fourth year of funding, we have accomplished the following tasks:

- Completed the 12 and 18 month visits.
- Determined the discontinuation rate by site for all completed visits.
- Completed the 24-month visit on 129 subjects.
- Completed audiotaping and a reliability analysis on 21% of all visits.
- Developed a protocol for recording menstrual calendar data.
- Developed visit-specific databases.
- Completed data entry, verification and cleaning of 3, 6, 12 and 18-month visits.
- Started preliminary analyses of data up to 12 months.
- Prepared and submitted two abstracts to major gynecologic societies. The first abstract, "**A prospective study of the effects of oral and injectable contraception on bone mineral density**" was presented orally at American College of Obstetricians and Gynecologists on May 22, 2000.

The second abstract titled, **"Condom practices prior to and after initiation of hormonal contraception"** will be presented at the annual meeting of Central Association of Obstetricians and Gynecologists October 21, 2000.

Conclusion

The fourth year of funding has been an active and successful period for the project. Twenty-four month study visits for all but 29 subjects have been completed. Data entry and verification for data up to 18 months has been completed. Preliminary analyses have begun for data up to the 12-month visit. Two abstracts presented to major gynecologic societies have resulted from this project.

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Menstrual Calendars Data Collection

Definitions:

Unit of observation - one day (not necessarily beginning and ending at midnight)
Bleeding - vaginal blood loss requiring sanitary protection
Spotting - vaginal blood loss not requiring protection
Bleeding day - day on which bleeding is recorded
Spotting day - day on which spotting alone is recorded

If spotting and bleeding occur on the same day, bleeding is the dominant event and the day is recorded as a bleeding day.

Nonbleeding day - day on which neither bleeding or spotting is recorded
Bleeding/spotting episode - any consecutive set of one or more bleeding and spotting days bounded at each end by two or more nonbleeding days

Bleeding/spotting days separated by only 1 nonbleeding day are considered part of the same bleeding/spotting episode.

If spotting occurs with bleeding (that is spotting is not bounded by at least two nonbleeding days) then it is counted as part of the bleeding/spotting episode.

Spotting episode - a consecutive set of one or more spotting days bounded by nonbleeding days
Nonbleeding interval - a consecutive set of two or more nonbleeding days bounded by bleeding or spotting days; a nonbleeding interval is terminated when the next bleeding/spotting or spotting episode begins
Episode - may consist of spotting days or bleeding/spotting days bounded by nonbleeding days (roughly synonymous to period)
Event - an episode and its consecutive nonbleeding interval (roughly synonymous to cycle)
Complete event - includes a bleeding/spotting or spotting episode and its corresponding nonbleeding interval
Incomplete event - a bleeding/spotting or spotting episode whose nonbleeding interval length cannot be determined as bleeding/spotting or spotting does not occur again (ammenorhea) or the subject discontinues and the next bleeding/spotting or spotting episode is not known

Rules

Reference periods begin at the first bleeding/spotting or spotting episode following initiation of contraception.
Complete episodes which overlap reference periods are included in the reference period where bleeding/spotting or spotting begins.

Events which are incomplete at the end of a 90-day reference period are truncated according to the following rules.

1. Participants record data for at least 21 days beyond the end of a reference period.
2. If the incomplete event is completed within 20 additional days (90 + 20 = 110) beyond the end of the reference period, its actual length is recorded.
3. If the event is not complete at the end of the additional 20 days, truncate it and count it as if it ended on the 20th day.

For data to be included in the calculation of a reference period, subjects must have recorded data for ≥ 61 days of the reference period.

Range must be ≥ 2 to be included in the analyses dataset. We will record range in the database for each subject regardless of whether the range is ≥ 2. Subjects will be recoded or excluded from the set at the time analyses are completed.

Data collection form for the menstrual calendars is on the next page.

Menstrual Calendar Data

Subject Number _____(4 digits; use leading zeros) **METHOD** _____ Completed by initials: _____

Reference Period (circle one) 1 2 3 4 5 6 7 8

Reference Period Start Date _____ Reference Period End Date _____
(Enter 4 digit year on both dates)

Truncated 0 (No) 1 (Yes)

Episode 1 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 2 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 3 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 4 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 5 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 6 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 7 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 8 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 9 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Episode 10 Bleeding/spotting Spotting Only
 # days contraceptive use _____
# of bleeding/spotting days or spotting only days _____
# of nonbleeding days _____

Total # Bleeding/spotting episodes _____
Total # spotting episodes _____
Total # nonbleeding intervals _____
Minimum Bleeding/spotting episodes _____
Minimum Spotting episodes _____
Minimum Nonbleeding intervals _____

Longest Bleeding/spotting episode (# days) _____
Longest spotting episode (# days) _____
Longest Nonbleeding interval (# days) _____
Maximum Bleeding/spotting episodes _____
Maximum Spotting episodes _____
Maximum Nonbleeding intervals _____

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 1 Apr 03

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports written for this Command. Request the limited distribution statement for the enclosed accession document numbers be changed to "Approved for public release; distribution unlimited." Copies of these reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

Encl

PHYLLIS M. RINEHART
Deputy Chief of Staff for
Information Management

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